AMENDMENTS TO THE CLAIMS

Applicants have amended claims 1, 9, 30, and 42 without any intention of disclaiming equivalents thereof, and Applicants have cancelled claims 16 and 43 without prejudice to their subsequent reintroduction into this application or their introduction into a related application. The following list of claims replaces all prior versions and lists of claims in the application.

Listing of Claims:

1. (Currently Amended) A method for achieving high sensitivity detection and/or high accuracy quantitation of a plurality of target proteins in a biological sample, at least one of which comprises the expression product of an alternative splicing form of a single DNA, the method comprising the steps of:

   (1) fragmenting proteins in the sample using a predetermined denaturation and proteolytic protocol to generate a solution of polypeptide analytes comprising recognition sequences comprising peptide epitope tags (PETs) displaying solvent accessible binding surfaces unambiguously indicative of the presence in the sample of the target proteins from which they are derived, at least one of which is unambiguously indicative of the presence in the sample of the alternative splicing form protein from which it is derived;

   (2) providing an addressable array of plural capture agents, which capture agents selectively interact with a peptide epitope tag (PET) of said target ~~protein to unambiguously indicate the presence of said target protein in the sample~~ proteins including a peptide epitope tag (PET) unambiguously indicative of the presence in the sample of said alternative splicing form protein;

   (3) contacting said array with said solution to capture polypeptide analytes by binding interaction between respective capture agents and said PETs presented by respective said analytes; and,

   (4) detecting the presence and amounts of said target proteins in the sample by detecting said captured polypeptide analytes with secondary capture agents specific for captured polypeptide analytes and labeled with a detectable moiety.

2. (Previously Presented) The method of claim 1 comprising providing an addressable array of capture agents comprising plural capture agents which selectively interact with different PETs from the same target protein and quantitating, if present, the amount of the target protein in the sample by averaging the results obtained from each said capture agent.

3. (Previously Presented) The method of claim 1 wherein said capture agents comprise antibodies.

4. (Previously Presented) The method of claim 1, wherein said capture agent comprise a member selected from the group consisting of non-antibody polypeptide, PNA (peptide nucleic acids), scaffolded peptide, peptidomimetic compound, polynucleotide, carbohydrates, artificial polymers, plastibody, chimeric binding agent derived from low-affinity ligand, and small organic molecules.

5. (Previously Presented) The method of claim 1, wherein said secondary capture agents bind to an epitope on a said polypeptide analyte separate from said solvent accessible binding surfaces.

6. (Previously Presented) The method of claim 1, wherein a subset of said capture agents bind to the same PET.

7. (Original) The method of claim 1, wherein said target protein has two or more different forms within said biological sample.

8. (Original) The method of claim 7, wherein said different forms include unprocessed / pro-form and processed / mature form.

9. (Currently Amended) The method of claim 1 wherein said peptide epitope tag (PET) unambiguously indicative of the presence in the sample of said alternative splicing form protein comprises an amino acid sequence comprising a splice junction ~~7, wherein said different forms include different alternative splicing forms~~.

10-12. (Canceled)

13. (Previously Presented) The method of claim 7, further comprising determining the percentage of one form of said target protein as compared to the total target protein, or ratio of a first form of said target protein to a second form of said target protein.

14-18. (Canceled)

19. (Original) The method of claim 1, wherein said sample is a body fluid selected from: saliva, mucous, sweat, whole blood, serum, urine, amniotic fluid, genital fluid, fecal material, marrow, plasma, spinal fluid, pericardial fluid, gastric fluid, abdominal fluid, peritoneal fluid, pleural fluid, synovial fluid, cyst fluid, cerebrospinal fluid, lung lavage fluid, lymphatic fluid, tears, prostatitc fluid, extraction from other body parts, or secretion from other glands; or from supernatant, whole cell lysate, or cell fraction obtained by lysis and fractionation of cellular material, extract or fraction of cells obtained directly from a biological entity or cells grown in an artificial environment.

20. (Previously Presented) The method of claim 1, wherein said sample is obtained from human, mouse, rat, frog, fish, fly, nematode, fission or budding yeast, or plant.

21. (Original) The method of claim 1, wherein said sample is produced by treatment of membrane bound proteins.

22. (Canceled)

23. (Previously Presented) The method of claim 1, wherein said secondary capture agent is labeled with a detectable moiety selected from: an enzyme, a fluorescent label, a stainable dye, a chemilumninescent compound, a colloidal particle, a radioactive isotope, a near-infrared dye, a DNA dendrimer, a water-soluble quantum dot, a latex bead, a selenium particle, or a europium nanoparticle.

24. (Previously Presented) The method of claim 23, wherein said secondary capture agent is labeled with a fluorophore.

25. (Canceled)

26. (Original) The method of claim 1, wherein said sample contains billion molar excess of unrelated proteins or fragments thereof relative to said target protein.

27. (Original) The method of claim 1, wherein said PET is identified based on one or more of the protein sources selected from: sequenced genome or virtually translated proteome, virtually translated transcriptome, or mass spectrometry database of tryptic fragments.

28. (Previously Presented) The method of claim 1, wherein one or a combination of said target proteins serve as a biomarker.

29. (Canceled)

30. (Currently Amended) An array of capture agents for detecting and quantitating plural target splice variant proteins comprising the expression products of one or more splice variants of a single DNA within a biological sample, the array comprising a plurality of capture agents, each immobilized on a distinct addressable location on a solid support, plural of said capture agents specifically binding to recognition sequences comprising peptide epitope tags (PETs) displaying solvent accessible binding surfaces unambiguously indicative of the presence in the sample of the proteins from which they are derived that predictably results from a treatment of said biological sample.

31. (Previously Presented) The array of claim 30, wherein said solid support comprises beads or an array device comprising features disposed in a manner that encodes the identity of said capture agents disposed thereon.

32. (Previously Presented) The array of claim 30, comprising 2 - 100 or more different capture agents.

33. (Previously Presented) The array of claim 30, wherein a said capture agents is a single chain antibody.

34. (Previously Presented) The array of claim 30, wherein a said capture agent is an antibody or antigen binding portions thereof.

35-41. (Canceled)

42. (Currently Amended) A method for detecting in a biological sample the presence of plural target proteins, at least some of which ~~comprising~~ comprise an expression product of one or more splice variants of a single DNA, the method comprising the steps of:

(1) fragmenting proteins in the sample, using a predetermined denaturation and proteolytic protocol, to generate a solution of polypeptide analytes comprising recognition sequences displaying solvent accessible binding surfaces unambiguously indicative of the presence in the sample of splice variant proteins from which they are derived;

(2) providing an addressable array of plural capture agents which selectively interact with binding surfaces of said polypeptide analytes;

(3) contacting said array and said solution to capture polypeptide analytes by binding interaction between respective capture agents and said binding surfaces presented by respective said analytes; and,

(4) detecting the presence of said target splice variant proteins in the sample by detecting ~~said binding interactions~~ said captured polypeptide analytes with secondary capture agents specific for captured polypeptide analytes and labeled with a detectable moiety .

43. (Canceled)

44. (Previously Presented) The method of claim 42, wherein the addressable array of capture agents comprises plural capture agents which selectively interact with different solvent accessible binding surfaces from the same target splice variant proteins.

45. (Previously Presented) The method of claim 44, further comprising quantitating, if present, the amount of a target splice variant protein in the sample by averaging the results obtained from each said capture agent.

46. (Previously Presented) The method of claim 42, wherein said capture agents comprise antibodies.

47. (Previously Presented) The method of claim 6, wherein said subset of said capture agents have different affinity and/or avidity for said same PET.